

A Pilot Double-Blinded, Randomized, Clinical Trial of Topical Virgin Olive Oil Versus Piroxicam Gel in Osteoarthritis of the Knee

Shahab Bohlooli, PhD,* Marina Jastan, MD,† Babak Nakhostin-Roohi, PhD,‡
Sadollah Mohammadi, PharmD,* and Zahra Baghaei, RN,*

Osteoarthritis (OA) is the most common type of arthritis, and the knee is the most common site of symptomatic OA.¹ Knee OA is responsible for a higher incidence of disability than any other long-term conditions.² Topical therapies present a therapeutic option for OA pain management. Nonsteroidal anti-inflammatory drugs (NSAIDs), salicylates, and capsaicin are currently the main topical therapies available.³ There is a need for safe and effective drugs for patients who do not respond well to conventional medical therapy. Indeed, such patients are turning increasingly to complementary/alternative medicines.^{4,5}

One of the traditional methods for management of knee pain in some rural area of Iran is application of topical olive oil, as reported by Avicenna⁶ in his 10th-century book *Canon of Medicine*. Although the composition of olive oil is complex, the major groups of compounds thought to contribute to its observed health benefits include oleic acid, phenolics, and squalene,⁷ all of which have been reported to inhibit oxidative stress.⁸ Researchers reported beneficial effects of olive oil on rheumatoid arthritis after oral consumption.⁹ In 2005, (–)-oleocanthal, the dialdehydic form of (–)-deacetoxy-ligstroside aglycone present in freshly pressed extra virgin olive oil, was shown to have properties of an NSAID.¹⁰

Although topical virgin olive oil is traditionally used in Iran in treating knee pain as an herbal medication, our survey did not find any scientific evaluation of its efficacy. Accordingly, we conducted a pilot prospective, comparative, randomized, double-blinded trial of topical virgin olive oil therapy versus piroxicam gel in the treatment of knee OA. The report was prepared as recommended by the CONSORT statement^{11,12} and its elaboration on herbal interventions.¹³

MATERIALS AND METHODS

Trial Design

This was a 4-week, balanced randomization (1:1), double-blind, standard controlled, parallel-group, phase 2 pilot trial conducted in Ardabil, Iran. After enrollment, eligible patients underwent 1-week (or at least 5 half-lives, whichever was longer) washout of analgesics before being randomized to receive piro-

xicam or olive oil daily for 4 weeks. After a baseline visit, patients returned to outpatient clinic on weeks 1, 2, 3 and 4 for assessment of efficacy, safety, and compliance. The study was approved by the university ethical board as well as consistency with principles of the Declaration of Helsinki. All the patients gave a written informed consent. The study was also registered with ClinicalTrials.gov (identifier NCT00670475).

Changes to Trial Design

Although the trial was approved to include both sexes, the low recruitment rate of male patients skewed the study, and it was changed to only female sex. Initially, the study design was on 100 patients on each arm, but based on accumulating data from participants' outcomes, which were monitored by an independent body without breaking the blindness, and unexpected long duration of study that led to financial limitation, a recommendation was applied to reduce the sample size to 30 patients on each arm.

Settings and Participants

The study took place at the rheumatology clinic of Imam Hospital, Ardabil University of Medical Sciences, Ardabil, Iran, from April 2008 to April 2010. Participants were eligible if they were female adults aged between 40 and 85 years with a diagnosis of OA of 1 or both knees according to the American College of Rheumatology criteria and a flare of pain after withdrawal of prior therapy with either an oral NSAID or acetaminophen (used at least 3 d/wk during the previous month). Key requirement for randomization at the baseline visit was a Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale score of 9 or higher on a 20-point scale.¹⁴ Pain was scored at the screening visit, after which prior therapy was withdrawn. The patient scored the pain again at the baseline visit. A flare was defined as an increase in total pain subscale score of at least 2 during the screening and baseline visits.

Patients were excluded from the study if they had secondary arthritis related to systemic inflammatory arthritis; corticosteroid use, ongoing use of prohibited medication including NSAID, other oral analgesic, muscle relaxant, or low-dose antidepressant for any long-term pain management; ongoing use of glucosamine or chondroitin, a sensitivity to NSAIDs, acetaminophen, dimethyl sulfoxide, propylene glycol, glycerine, or ethanol; clinically active renal, hepatic, or peptic ulcer disease, history of alcohol, or drug abuse; lactation; concomitant skin disease at the application site; and current application for disability benefits on the basis of knee OA, fibromyalgia, other painful, or disabling condition affecting the knee.

Randomization and Interventions

After the washout period, eligible patients randomized in 1:1 ratio to receive piroxicam or virgin olive oil. The gel of

From the Departments of *Pharmacology and †Rheumatology, School of Medicine, Ardabil University of Medical Science; and ‡Department of Exercise Physiology, Ardabil Branch, Islamic Azad University, Ardabil, Iran.

This study was financially supported by a research grant from Ardabil University of Medical Sciences.

The authors declare no conflict of interest.

Correspondence: Shahab Bohlooli, PhD, Department of Pharmacology, School of Medicine, Ardabil University of Medical Science, University Street, Ardabil, 56197, Iran. E-mail: shahab.bohlooli@arums.ac.ir.

Copyright © 2012 by Lippincott Williams & Wilkins

ISSN: 1076-1608/12/1802-0000

DOI: 10.1097/RHU.0b013e31824a47b5